

**PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of )  
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ROBERT J. LIPSHUTZ et al. )  
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Application No.: Unassigned )  
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Filed: Herewith )  
 )  
For: POLYMORPHISM DETECTION )  
 )  
\_\_\_\_\_ )  
 )

Examiner: J. Riley  
Art Unit: 1656  
August 24, 2001

CERTIFICATE OF EXPRESS MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under CFR § 1.10 on the date indicated below and is addressed to: Assistant Commissioner for Patents, Washington, DC 20231 on August 24, 2001.

Signed: \_\_\_\_\_

Jack L. Limper

AMENDMENT A

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to the examination of the application on the merits, please amend the application as follows.

In the Specification

Please replace the paragraph beginning on page 1, line 6 with the following:

This application is a continuation of 08/853,370, filed May 8, 1997, which is a continuation-in-part of 08/563,762, filed November 29, 1995, and claims the benefit of U.S. provisional application 60/017,260, filed May 10, 1996, the disclosures of which are incorporated by reference in their entirety for all purposes.

Please replace the paragraph beginning on page 4, line 23 with the following:

e) using principal component analysis, identifying a polymorphism by comparing normalized differences between individuals in a population.

Please replace the paragraph beginning on page 4, line 30 with the following:

Figure 2A shows a schematic representation of a single oligonucleotide array containing 78 separate detection blocks. Figure 2B shows a schematic illustration of a detection block for a specific polymorphism denoted WI-567 (TGCTGCCTTGGTTCRAGCCCTCATCTCTTT, SEQ ID NO:1). Figure 2B also shows the triplet layout of detection blocks for the polymorphism employing 20-mer oligonucleotide probes having substitutions 7, 10 and 13 bp from the 3' end of the probe (AACCAANCTCGGGAGTAGAG, SEQ ID NO:2; CGGAACCAANCTCGGGAGTA, SEQ ID NO:3; CGACGGAACCAANCTCGGGA, SEQ ID NO:4). The probes present in the shaded portions of each detection block are shown adjacent to each detection block.

Please replace the paragraph beginning on page 5, line 1 with the following:

Figure 3 illustrates a tiling strategy for a polymorphism denoted WI-567, and having the sequence 5'-TGCTGCCTTGGTTC[A/G]AGCCCTCATCTCTTT-3' (TGCTGCCTTGGTTCRAGCCCTCATCTCTTT, SEQ ID NO:1). A detection block specific for the WI-567 polymorphism is shown with the probe sequences tiled therein listed above (ACGGAACCANGTTCGGGAGT, SEQ ID NO:5; ACGGAACCANGCTCGGGAGT, SEQ ID NO:6; CGGAACCAANTTCGGGAGTA, SEQ ID NO:7; CGGAACCAANCTCGGGAGTA, SEQ ID NO:8; GGAACCAAGNTCGGGAGTAG, SEQ ID NO:9; GAACCAAGTNCGGGAGTAGA, SEQ ID NO:10; GAACCAAGCNCGGGAGTAGA, SEQ ID NO:11; AACCAAGTTNGGGAGTAGAG, SEQ ID NO:12; AACCAAGCTNNGGGAGTAGAG, SEQ ID NO:13). Predicted patterns for both homozygous forms and the heterozygous form are shown at the bottom.

Please replace the paragraph beginning on page 5, line 8 with the following:

Figure 4 shows a schematic representation of a detection block specific for the polymorphism denoted WI-1959 having the sequence 5'-ACCAAAAATCAGTC[T/C]GGGTAACTGAGAGTG-3' (ACCAAAAATCAGTCYGGGTAACTGAGAGTG, SEQ ID NO:14) with the polymorphism indicated by the brackets. A fluorescent scan of hybridization of the heterozygous and both

homozygous forms are shown in the center, with the predicted hybridization pattern for each being indicated below.

On page 7, line 36, before the period at the end of the sentence, please add --polymorphisms--.

On page 8, line 17, please delete "Serial" from the line.

On page 8, line 31, please change ""ESTs"," to --"ESTs,"--.

On page 9, line 18, please change "i.e." to --i.e.,--.

On page 9, line 21, before "is" please add --it--.

On page 17, line 16, please change "negative" to --positive--.

On page 17, line 24, please change "positive" to --negative--.

On page 19, line 31, before "with" please add --

(ACCAAAAATCAGTCYGGGTAAGTGAAGTG, SEQ ID NO:2)--.

On page 21, line 19, please change "1:27-35." to --1:27-35--.

Please insert the attached pages numbered 27-30 and entitled "SEQUENCE LISTING" following page 26 of the specification and renumber original pages 27-30 sequentially as 31-34.

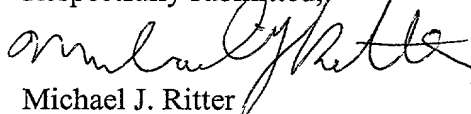
#### In the Claims

Please cancel claims 8-17 without prejudice.

#### REMARKS

Claims 1-7 are pending in the application. Applicants canceled claims 8-17 but reserve all right to pursue these or other claims in a continuing application. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 446-8693.

Respectfully submitted,



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**VERSION WITH MARKINGS TO SHOW CHANGES  
MADE TO THE APPLICATION**

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FOR "SECRET"